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THE SEARCH FOR HEALTH

A Report from
The National Institutes of Health
Bethesda, Maryland

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From Impaired Glucose Tolerance to Diabetes: A Two-Step Process

For some time doctors have known that about 25 percent of adults with impaired glucose tolerance (IGT), a mildly abnormal rise in blood sugar levels, go on to develop severe glucose intolerance in the form of non-insulin dependent diabetes (NIDDM). It is also well known that overweight adults, especially those with a family history of diabetes, are at high risk for NIDDM (also called adult-onset or type II diabetes). However, one question that has puzzled doctors about impaired glucose tolerance is whether it, like diabetes, is marked by a failure to the pancreas to produce enough insulin, the hormone that regulates glucose metabolism. A research paper published in the May 12, 1988, issue of the *New England Journal of Medicine* answers that question by showing that overweight adults with impaired glucose tolerance have normal, functioning pancreas glands able to produce very high levels of insulin. Even when exposed to large amounts of insulin, though, their bodies' tissues do not efficiently use blood sugar, a condition known as "insulin resistance."

"Insulin resistance, not insulin deficiency, is the abnormality underlying IGT," said Dr. Stephen Lillioja, who headed the team of researchers from the National Institute of Diabetes and Digestive and Kidney Diseases. "The good news is that the pancreas still seems to be healthy and can make insulin. Often, weight loss alone can improve insulin's effectiveness. But if nothing is done to improve its effectiveness, the pancreas may give up and stop responding to glucose in the bloodstream, and diabetes will develop." Insulin resistance appears to be a defect in the way muscles respond to insulin in the blood, a trait that seems to run in families. Obese

Moderate levels of glucose in the blood signal the pancreas to secrete more insulin, but it is likely that high levels of glucose damage beta cells, the insulin-producing cells of the pancreas. For this reason, preventing diabetes by treating IGT is much better than treating diabetes once it develops, Lillioja added.

Lillioja and colleagues arrived at their conclusion after studying insulin action and secretion before and after the development of impaired glucose tolerance in a group of 24 adults and in 254 other adults with the whole range of glucose tolerance, including frank diabetes. Insulin's ability to act was measured by a technique in which insulin and glucose were infused into a vein. Normally, the blood glucose level falls when a person is given insulin. In people whose insulin is effective, a large amount of glucose is needed to prevent this fall. When insulin is ineffective, little glucose is needed despite high concentrations of insulin in the blood. The researchers found that in people with impaired glucose tolerance insulin was relatively ineffective. In people with diabetes, however, the action of insulin was even more impaired, and pancreatic function had declined.

In doctors' offices, the oral glucose tolerance test is used to determine how well a person regulates blood sugar levels. Impaired glucose tolerance is diagnosed when a person's blood sugar levels exceed normal in reponse to a premeasured dose of glucose but are not high enough to meet the definition of diabetes.

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